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viewpoint

Challenges to informed consent

New developments in biomedical research and healthcare may mark the end of the traditional concept of informed consent

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New scientific discoveries and new technologies soon challenge our old ways of proceeding and thinking. It is no surprise then that new knowledge in molecular genetics and the ensuing developments in genetic technology bring with them new modes of thought, not just in science and medicine, but also in ethics, law and public policy. One tradition that is being challenged at the moment is the notion of informed consent. This concept, with its emphasis on individual autonomy, personal decision-making and the protection of privacy, is at the centre of medical ethics and law. However, advances in genetics and biomedical research as well as new forms of decision-making in healthcare may well require a rethinking of this traditional idea.

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Informed consent applies to two related, but nevertheless different, settings: medical practice and biomedical research on human tissues and health information. First, it is at the heart of the relationship between doctor and patient. Before initiating a procedure or treatment, a doctor must inform his or her patient of the details, importance, consequences and risks that this treatment entails, and must seek their consent before proceeding. In rare cases, when the patient is not able to give consent, this must be sought from the next of kin. The second setting is medical research, where informed consent is mandatory before extracting or using an individual's biological material, be it cells, tissues or organs. Only by clearly explaining to this person how the biological material will be extracted and used, and obtaining their consent to these uses, can researchers proceed both ethically and legally.

Some aspects of genetic diseases have already revealed shortcomings of the notion of informed consent as it is generally understood. For example, various perceptions of 'adequate information', that are at the heart of informed consent, are at odds with the complexity of genetic information, metabolic processes and pathways, and particularly the uncertainties about the causal influence of environmental versus genetic factors in disease expression. The human difficulty in comprehending probability reasoning also adds challenges to the concept of being 'well informed'. Furthermore, the lack of training in genetics for physicians and the shortage of genetic counsellors have increased doubts about the 'informational' component of consent.

A second challenge is the fact that genetic information often has an impact on people other than the patient and thus is, in some sense, 'shared' information. Traditional informed consent, however, assumes that any decisions that are made concern the values and life of a single individual. The 'I inform, you consent' model presumes that a rational individual physician or researcher is informing a rational individual subject, who will then give his or her 'informed' consent. Clearly, a diagnosis for Huntington's disease, or finding mutations that drastically increase the risk of developing breast cancer, not only affect the patient, but equally his or her children, partner and close relatives. It raises the question of whether such information should be limited to the patient, or whether there is an obligation to inform others who may also be at risk.

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Limiting informed consent to the individual also does not acknowledge the fact that most people make decisions in concert with, or in relation to, their significant others. The traditional model fails to recognize that an individual is also a social person with a particular historical and socio-cultural context giving that person certain ways of viewing things, as well as a set of values. Each person has their own understanding of who they are, how they and others should be treated as people, and what important relationships need to be honoured. Each individual also has their own views about disease and illness and will face genetic issues with their own level of fears, concerns and questions. Different ethnic groups and cultures have different ways of interpreting consent, disease and illness. Finally, the traditional

model of informed consent also fails to recognize that certain people, especially authority figures, such as physicians and researchers, have a level of social status and power that may well have an impact on the patient's decisions or their ability to make such decisions. Thus, informed consent is already perceived to be an imperfect instrument of protection—even in regular medicine—and some have proposed abandoning the concept.

The latest challenge to informed consent, and perhaps the most serious set of problems, comes from the development of various DNA databases. Harvard epidemiologist Walter Willett and his colleagues, for example, are pooling data from large cohort studies such as the Harvard Nurses' Health Study, the American Cancer Society and the European Prospective Investigation into Cancer and Nutrition. This combined database will provide more than 1 million DNA samples for cancer research. A similarly focused database at the International Diabetes Institute (Melbourne, Australia) holds tissue samples and information from more than 30,000 individuals. Another type of focused DNA database collects DNA for purposes of law enforcement and the judicial system. Various concerns about privacy, one of the rights presumably protected by informed consent, have been raised in relation to these DNA databases. Discussions have focused on lessened rights of privacy and consent and on the interests of the state and community versus those of the individual (Rooker, 2000).

Even more at the forefront of challenges to the notion of informed consent are the new population DNA databases. For example, Michael Caldwell, Director of the Marshfield Clinic Research Foundation in Wisconsin, USA, is seeking 40,000 participants to donate their DNA for research focused on the links between genes, lifestyle factors and illness (Kaiser, 2002). Of even greater importance are the DNA databases being established by several countries for their entire populations. The two primary goals of these efforts are to improve the healthcare of the population and to conduct population studies of the genetics of common disease. Iceland and Estonia are leading this movement, and the UK and Latvia are also undertaking such projects. Another, very controversial, plan for such a database has been proposed for the Pacific archipelago of Tonga.

Informed consent usually covers only specific and known uses of biological material—for example, when a person consents to their DNA being used in a particular experiment or research study. For other situations in which material may be used more than once, or for as yet unknown research, other forms of consent have been devised. Open, or blanket, consent is given only once, but covers any use of the material at any time in the future. This is particularly important for scientific research, in which new projects or experiments might be devised years after individuals have given their consent and deposited their biological material; they may even have died in the meantime. Informed consent is given only after the patient or participant in a study has received information about the planned use of the material and healthcare data. Presumed consent, conversely, assumes that an individual agrees in principle to their material being used for any reason: if not, they must withdraw their consent, or 'opt out'. Presumed consent may be easier to obtain, but understandably can alienate participants, who may resent their involuntary involvement.

Consequently, the usual informed, specific consent that a doctor receives from a patient may not be applicable to ventures that combine research and healthcare goals. Iceland, for example, provides assumed or presumed consent with a provision for people to opt out. Estonia asks their citizens for open consent when they provide blood samples and healthcare information to the database. The controversy surrounding the proposed Tonga database also raises the question of whether developed countries should seek to impose an ethical or legal viewpoint on other countries with differing views of the consent process. The argument is that informed consent in developed countries has focused too long on medicine and individual autonomy, but has failed to take account of the equal values of community, solidarity and mutual security.

Informed consent, as it is generally understood, rests on the principle of autonomy, or the right to self-determination. Self-determination usually means that each person takes responsibility for his/her own actions and, in the context of health care, has a right to determine what will be done with his/her own body. This emphasis on the right of determination sets the initial legal context for violation of informed consent in tort law. The focus now, however, is on negligence and the failure to adequately inform patients of the nature and possible consequences of the procedure that is to be carried out. What, then, is adequate information? Two standards have generally been applied to make this determination. One is the professional custom standard, known in the British legal system as the Bolam principle. The question of sufficient information is tested against the current opinions of an informed body of medical practitioners (for criticisms of the Bolam principle, see Kirby (1995) and Fenwick & Beran (1996)). The second standard, put forward in *Canterbury v Spence* (1972; US Court of Appeals, District of Columbia Circuit), is known as 'the prudent person test'. According to this test the information given to a patient must be sufficient to satisfy and fully inform a prudent or reasonable patient so that they can decide whether or not they desire treatment.

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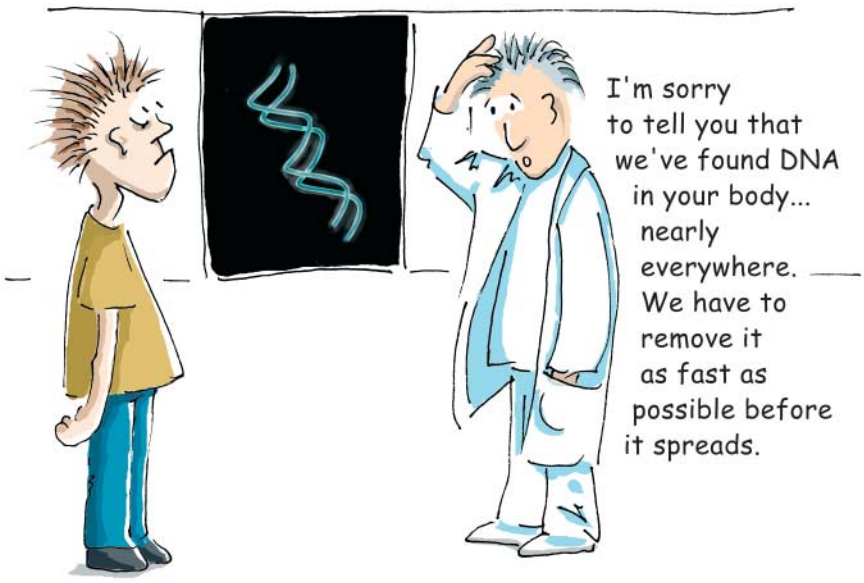
Although these two criteria of adequate information have been operative in the law on informed consent, both have been criticized for their inadequacies. The main objection to the professional custom rule is that it gives too little attention to the patient's concerns and values. The weakness of the reasonable patient criteria is its emphasis on a generalized notion of what is rational and a neglect of patient individuality and variability. A third standard has been proposed and used in the USA: namely, the subjective substantial disclosure rule. This states that adequate information is information that would be material or important to the decision of this particular patient in this circumstance. A key question with this rule is: "Could this information change the decision of this particular person in



this particular circumstance?" Such a rule requires a substantial degree of knowledge about the patient, their situation, and what is important to them. It at least gives attention to the social and cultural context of the patient and allows consideration of the role of significant others in a patient's decisions. People are influenced in their decisions by the views of significant others and they are generally concerned about the impact of their decisions on the lives and health of those they know and care about. This concern is particularly relevant to dealing with genetic information, as already indicated.

Another weakness of the traditional informed consent procedure is that it is usually viewed as a 'single' episode in which the physician provides information and the patient or proxy indicates a choice, or consents to the physician's proposal. Further, informed consent is often given after only a short conversation occurring just before treatment. This single-minded focus and context does not adequately address the possibilities of important changes in information, treatment and diversification. The new emphasis on genetic predisposition to disease and prevention would therefore require an informed consent process that involves renewal and re-consultation, which is very much at issue with the developing population DNA databases.

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To understand the specific challenges posed to informed consent by the new population databases, we need to consider several examples. In 1998, deCODE Genetics (Reykjavík, Iceland), under contract with the Icelandic government, proposed placing the health records of all 270,000 citizens into a single database and combining it with Iceland's detailed genealogy and genetic data, collected from volunteers. Under a 12-year license, drug companies could access the data for a fee, while academic researchers could have free access. The most contentious aspect of this project is that it relies on presumed consent. Government health records on every citizen are included in the database unless individuals specifically request otherwise; in other words, unless they opt out of the project. It is estimated that about 9–10% of the Icelandic population has exercised this option. Presumed consent, of course, does not follow the traditional informed consent pattern of disclosure, comprehension, competence and voluntary consent or refusal. Furthermore, some argue that informed consent, in this case, has become a political act: only after extensive public debate, through an act of parliament, was public informed consent added to the project. Further confusion for the informed consent notion is that deCODE's project mixes both healthcare and research interests, thus causing uncertainty about the processes of informed consent, as those for standard healthcare differ from those in place for research purposes. In the Icelandic case, informed consent is mandated by the 2000 Biobank Act for samples collected for research studies, but assumed consent is allowed for health data and treatment. In fact, informed consent is not mandated under the 1998 Health Sector Database Act and the withdrawal of consent in the opinion of some falls short of standards such as those proposed by the World Medical Association (WMA) in recent declarations (WMA, 2002).

Estonia is in the process of establishing the Gene Bank, its own population DNA database. The government-funded, non-profit Estonian Genome Project Foundation is collecting DNA samples from 10,000 volunteers aged 16 years and over; health information on individuals is obtained in parallel using a questionnaire. The purpose of the Gene Bank is to enable "scientific and applied gene and health research to be carried out in order to find genes that influence the development of illnesses" (Estonian Genome Project Foundation, 2001). The rights of donors are regulated and spelled out in the Human Genes Research Act (2001). The gene donor is given an informed consent form, a copy of the law and an information kit. The collected data is encrypted and all information and other material given to researchers remain anonymous. The law protects from discrimination against a gene donor and stipulates a penalty. The gene donor has the right to access his or her data, as does a physician provided that he/she has the donor's consent. The donor is also given the right to genetic counselling on accessing his or her data, and has the right not to know his or her data. In the case of Estonia, the notion of the donor's informed consent has been honoured. However, in reality, it is open consent as the Estonian Genome Project Foundation is authorized to use the data for an open research agenda; that is, research shall not be limited to the present scientific level and can pursue ends other than those originally stated in the authorization for the Gene Bank.

The issue of open consent has also surfaced in connection with the database proposed by the UK Medical Research Council and supported by the Wellcome Trust charity. The BioBank project will gather DNA samples, medical history,

prescription histories and information from a lifestyles questionnaire from 500,000 volunteers aged 45–69 years. The purpose is to study the interactions of genetic and lifestyle factors in the occurrence of diseases. Researchers will have free access to the BioBank, and it is here that the concern for open consent develops. At the current time, the legal obligation of informed consent in a research setting is extensive. It requires—at a minimum—that information be provided on all potential risks and, more specifically, on the nature of the research protocol. It assumes that the donor maintains a basic interest in what happens to his or her health and genetic information, and in controlling access to it. Therefore, it would seem logical that re-consent to new directions of research would be required. However, with population research, the purpose and direction of the studies may not be fully known at the time that the samples and consent are obtained; but to obtain multiple requests for consent would over-burden both the researcher and the participant. The UK Human Genetics Commission therefore concluded that "the difficulties involved in tracing and securing re-consent for different forms of medical research may make obtaining fresh consent impractical and would seriously limit the usefulness of large-scale population databases" (UK Human Genetics Commission, 2002).

In light of these problems, the 2001 UNESCO Report on Collection, Treatment, Storage and Use of Genetic Data suggested that "blanket consent covering all forms of research might be preferable" (Rumball & McCall Smith, 2002). This seems to support the Estonian model, but others argue for the presumed consent model adopted by Iceland. Public surveys have indicated a strong desire for retention of the consent process for databases and have shown that people would prefer that fresh consent be sought from individuals before new research is conducted on existing DNA samples (UK Human Genetics Commission, 2000). Others contend that blanket consent falls far short of true informed consent as it is too vague and therefore would be of little use in legal proceedings. It also does not allow participants to act on their continuing interest in health information (Caulfield, 2002). Indeed, the latest statement from UNESCO on human genetic data says that "Prior, free, informed and express consent shall be required for the collection of human genetic data…" (UNESCO, 2003). This stance was confirmed by the Quebec Network of Applied Genetic Medicine, which stated that "Consent is a continuing process and must be reconfirmed for instance in the cases of significant changes to the research protocol, to the conditions of banking, in the research partnerships, and in the management of the bank" (Cardinal *et al*, 2003). Another alternative is to set up a new legal/ethical framework for dealing with population databases. One proposed model is the 'authorization' model, which would include permission for unforeseen research, re-contact of subjects, time limits on the use of samples, and information on potential implications for social groups and on commercial uses. This model also requires additional protections and a socially constituted, legally mandated oversight body (Greely, 1999).

The controversy surrounding the proposed gene database for Tonga brings to the fore another aspect of the challenge to informed consent, namely its narrow focus on biological medicine and individual autonomy, and its lack of attention to cultural diversity. In November 2000, the Australian biotech company Autogen (now part of ChemGenex Pharmaceuticals Ltd, Geelong, Victoria, Australia) announced that it had signed a contract with Tonga's Ministry of Health to gain exclusive rights to the entire gene pool of the Tongan people. In return, the company was to build a genetics-based research facility and to provide annual research funding to Tonga's Ministry of Health. Like Iceland, Tonga has an isolated population with rich genealogical data. There is also a high prevalence of certain diseases such as type 2 diabetes-related obesity and weight imbalance problems. Autogen has since abandoned its proposal, but important issues about informed consent related to this database should be noted. First, a standard informed consent procedure could not adequately address the unique process of group decision-making in the tightly knit, but acutely status-conscious, Tongan society. Group rights are important for the Tongan people because of their extended family groupings (*matakali*), which mean that genetic research implicates family genetic make-up. This also indicates a dissonance between a concept of individual genetic property and a notion of shared economic and cultural assets that is integral to an indigenous society like Tonga. Individual informed consent does not work for the Tongan culture because it is the extended family group that determines whether individual members are permitted to give informed consent.

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Second, there is the concern that a 'Western' ethical value system will be imposed on another culture with different values and views. There are differing cultural understandings of consent between collectivist and individualist-oriented societies. Thus, truthful disclosure may conflict with cultural beliefs about hope and wellness, and individual decision-making may counter family-centred values and the social meaning of competency.

The statement of the Bioethics Consultation in the Pacific, held in Nuku'alofa, Tonga, in March 2001 is instructive here. This statement strongly emphasizes the value of intra-generational relationships; it affirms that the peoples of the Pacific "are guardians of their heritage and have a right to protect and control dissemination of this heritage" (Senituli & Boyes, 2002), and it affirms the right of these people to manage their own biological resources and to preserve their traditional knowledge. The consultation was especially concerned about exploitation and expropriation. The concern is clearly that the scientific community in wealthy nations will acquire and use genetic samples and information about indigenous people, but will fail to share the ensuing wealth with those people (Senituli & Boyes, 2002).

In reviewing the new developments in genetic science and medicine, and particularly the development of population genetics databases, it seems clear that the old notion of informed consent becomes outdated and needs review. It is also not clear

yet whether the two main alternatives—presumed and open consent—will fare any better. Old rules often cannot fit new situations, and the changing needs, knowledge and globalization in biomedical and genetic research may demand a new ethical and legal framework for consent.

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